RATIONAL sRNA DESIGN FOR STRAIN ENGINEERING

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Harnessing global regulatory networks is a central goal in metabolic engineering for the production of industrially-relevant products. As an alternative to gene knockout and gene overexpression methods, several recent studies have proposed engineering of bacterial small RNAs for dynamic and fine-tuned control of gene expression. Given the importance of molecular structure to RNA functioning, sRNA engineering efforts depend heavily on the design of their specific shapes. Specifically, knowledge of the RNA structural accessibility landscape supports identification of interfaces relevant to regulation. In this talk, we will describe the development of our recently developed tools that allow for the simultaneous in vivo characterization of thousands of potential interacting interfaces in RNA molecules, as determined based on their molecular accessibility. We will describe the design of this synthetic probing approach and will showcase the potential of this method by presenting novel fundamental insights obtained for over 1000 interfaces in 72 bacterial sRNAs. The talk will also highlight our use of this high throughput structural profiling approach for the rational design of bacterial sRNAs to achieve a tunable gradient of global control for metabolic engineering applications. Our results suggest up to a 10-fold changes in sRNA activity after rational design of their submolecular structures. Altogether, our talk will aim to illustrate the potential of high throughput methods in informed, efficient design of global sRNA regulators for industrially-relevant phenotypes.